

SPL Process ER/DL Meeting

Meeting Minutes

July 15, 2015

Chair of today's meeting: Pat Cowall

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Teleconference information: How to mute/unmute

#6: Mute

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Link to the SPL wiki:

<http://spl-work-group.wikispaces.com/share/view/51351516>

Agenda:

1. **Export only SPLs.** What NDC product code to use (from Carl Strotz-Pfizer, Gail DiNicholas)
 - For export packs we used to use the same product code as the domestic formula, but some obscure packaging codes. That has tended to backfire as the US formulas get changed all the time. So we want to expire the US products from Dailymed while the overseas markets keep the formula for years because their registration timelines are so long. In the SPL world however, I assume a product has to either be a US finished good OR an export only product, but the same labeler/product code combination can't be both.
 - Assuming that much is right, two questions.
 - When you are listing export products, do you give them a completely different product code than the same product being sold in the US?
 - Also, if you are exporting the same product to two different countries, do you use the same product codes with different packaging codes or do you assign different product codes to each?

Situation 1: Export only drug listing. Marketing category is "export only." Doc type is appropriate whatever you are drug listing... "human pharma...etc"

- Created its own NDC. Used export only marketing classification.
- Where does it appear?
 - Will **not** appear in Daily Med. Does not appear in the NDC directory.
 - It is in the FDA data base .
- How do you know if it is valid?
 - Look for acknowledgement from FDA.
 - You can also contact the eDRLS group, they can confirm if it is valid.

Situation 2: US product that is mfg in US. Canadian affiliate is also manufacturing a product.

- Some companies have been told to drug list twice. (Atlanta and New York ports seem to expect this).
 - Drug list for the US manufacturer/PLD
 - Drug List for the Canadian site (using its own labeller code).
- Some companies have only drug listed once, since the foreign site is owned by the same company.
- Clarify: If adding an alternate site, the PLD needs list all the manufacturer

Note: FDA is getting stricter about giving out additional labeller codes for OUS affiliates.

2. Drug list API (Marcia)

For products that were sourced and manufactured in a foreign country with only the finished products imported into the US. The question was whether or not the API and/or excipient suppliers need to complete FDA establishment registrations if they only provided supplies to the manufacturer in the foreign country (not via the US).

- Overall: If the finished product manufacturer is marketing the products to the US, then they would need to list the product and include the foreign API manufacturer on the listing SPL (Herb sent this Q & received A from eRDLS)

The API is manufactured outside of the US and provided to another manufacturer outside of the US who produces the finished drug product and exports the finished product into the US (the API never touches the US except in the finished form).

- The foreign manufacturer of the finished product is a registered establishment.
- Does the foreign manufacturer of the API (who supplies the API to the finished product foreign manufacturer) need to be a registered establishment with the FDA even though they do not send the API to the US?

Response from eRDLS:

Is the finished product manufacturer marketing the products to the US? If yes, then they would need to list the product and include the foreign API manufacturer on the listing SPL.

Q/A from Lonnie:

Q: Is it a requirement or suggested best practice if there has been an update to the API Manufacturer that we are listing in the establishment portion of the SPL, if there is no content of labeling changes, should we be submitting an update to reflect the API change as soon as possible, or could we wait until the next content of labeling change happens to make this update?

A: If the product is regulated by CDER, it is not a requirement that you include the API manufacturer in the drug listing SPL file with information about the finished dosage form product.

Ruth: Validation guidelines do not require API. As of last July, customs groups are looking for the API to be in the drug listing file. They are looking for assurance that the API mfg is included in the registration.

- **Real Life-- Finished Products: Some** FDA inspectors at the port require that the API be drug listed also- if the API is manufactured outside the country. (Notes from 4/22/2015 meeting. Atlanta, Chicago, New York, Philly). CDER based products. Not CBER yet.
 - API needs a separate drug listing from the API site.
 - Final product needs to be drug listed from the finished site.
 - Foreign manufacturer needs to be drug listed.
 - The need for this drug listing may depend on the port of entry.
 - Atlanta requires this.

FDA officer does not see the API information on the final SPL. That is why they want the separate API listing.

Reminder:

API manufactured in the US and sent out of the US for manufacturing. Does the API require drug listing? All API sent out of the US should be drug listed. This is really important in case it ever would need to be returned to the US.

3. Drug listing – private label distributors. Marcia.

I had another question come up yesterday about drug listing when a PLD is involved. A company is the PLD and gets the finished product from a supplier. The company does the drug listing but has been told that the manufacturer is also required to list.

When I look at the FDA guidance:

(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072339.pdf>, page 7), it seems as if this request is counter to my read of the drug listing process. Am I interpreting the guidance correctly that if PLD lists the product, the manufacturer should NOT list the same product? If so, I was asked to see if any other company had received a similar request. And if this is not the procedure, it would be helpful to have any regulatory citation or a guidance to share with the company

If everything is in the US, then only one has to drug list- either the PLD or the manufacturer . But this is using the PLD labeler code.

If foreign, then the manufacturer DOES have to drug list using its own labeler code.

4. Imports/exports of vaccines. Tiffany (Merck)

- Issue 1: Importing bulk vaccine (for US market). CBER does not require drug listing bulk for import.
- Issue 2: Exporting bulk antigen (for foreign market).
- Drug listing as “bulk” and not as “vaccine”.

- Want to know why they are getting validation issues – stating that should be using “vaccine”. Possibly because not requiring for vaccine.
5. Ben: How to create a kit for a vaccine (10 vials of vaccine and 10 vials of saline). Saline has its own NDC number. See these examples on Daily Med.
1. Pegintron

We have a non-vaccine (BLA to CDER not CBER). It’s a vial of product plus diluent co packed - considered a kit. I don’t know if having the same inner NDC in different kits is a problem for CBER. I hope not. Not sure

<http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b70816bb-913a-467f-acb8-67ef62cf8dac>

This product has a lot of pkg configs – so look at the following NDCs

NDC:0085-4353 (diluent has NDC 0085-4346)

NDC:0085-4354 (diluent has the same NDC as above 0085-4346)

NDC:0085-4355 (ditto)

NDC:0085-4356 (ditto)
 1. Glucagon (NDA)
 2. Enbrel (BLA)
6. Lot Distribution Data SPL implemented on June 10, 2015 (from an SPL technical perspective)
- Make some minor tweaks based on feedback – to validation procedures
 - Difficult situations:
 - When kit is tracked as a package lot: hard. Lonnie will be developing an ebook to explain how to do this.
 - When there is a variable dose. Don’t enter dose.
 - Submitted through Module 3 of the eCTD.
7. Update from SPL Leadership meeting (Lonnie):
- a. New telephone numbers and pass codes. Tech team meetings on 1st and 3rd Mondays of each month. Also, training sessions. New pass code every time. Need to sign up.
 - b. Another FDA agency found 35 documents with “Human RX labeling without highlighting”. Lonnie will be following up with these companies.
 - c. Import/export: CPP (certificate of clinical product) group (everyone wanting to export a product) is requesting that they submit an SPL file with category export only. Issue is only with export products only – ie not for products that are also sold in this country.
 - Delay in issuance of certificates if don’t have this.
 - d. Wholesaler SPL file: that group needs out of business notification code for companies that no longer do this type of business. – have new LOINC codes.
 - e. SPL vendor training session – needs to be one in July and August – for wholesaler and other new stuff.
 - f. SPL stylesheet – slight issue with LDD.
 - LDD data was not rendering right, but not updating because want to see if anything is broken.
 - g. IG: updated in December. Need to update – but waiting for more LDD issues.

- h. SPL schema: dilemma because of recent R6 approval. Waiting to post this schema until after the out of ballot with R7, which is coming soon.
8. D&B feedback:
- Please send me any feedback for working with D&B. We were going to send out a survey, to help the cause. However, things seemed to have settled down – or people are learning to deal with it.
 - DUNS and SPL data is being used much more widely.
 - Starting to be used for customs/import/export – so it would be good to make consistent within your company.
9. Footnote eight in the draft Guidance for Industry – Compounding **Animal** Drugs from Bulk Drug Substances
(<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM446862.pdf>)
- “FDA has issued a draft guidance for industry, *Electronic Drug Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (November 2014), which prescribes how human drug compounding facilities are to submit drug product reports to FDA. Available at <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM424303.pdf>. Although this guidance addresses reporting of compounded human drug products, outsourcing facilities should follow the same procedure to electronically report the animal drug products they compounded.”
10. Other business
- REMS@FDA now up and running DDI webinar on REMS&FDA - June 23, 2015 at 1pm: <http://www.fda.gov/aboutfda/workingatfda/fellowshipinternshipgraduatefacultyprograms/pharmacystudentexperientialprogramcder/ucm447983.htm>
 - <https://www.federalregister.gov/articles/2015/06/19/2015-15076/guidance-for-industryand-staff-size-shape-and-other-physical-attributes-of-generic-tablets-and> FDA Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules; Guidance for Industry; Availability; Notice FDA is announcing the availability of a guidance for industry entitled "Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules." This guidance discusses FDA recommendations for the size, shape, and other physical attributes of generic tablets and capsules intended to be swallowed intact. FDA is concerned that differences in these physical characteristics between generic drugs and the originator drug could affect patient outcomes.
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM377938.pdf> Guidance

Next Meeting: July 29th (Herb chairing). Topic: IDMP Intro and Overview

This will be a webex, from Lync, accessed through Outlook. Look for the meeting invitation/announcement. You may have to do some setup prior to the meeting.

Future topic:

Product Concept Indexing SPL document

- Contains active ingredient, active moiety, dosage form, strengths. Intended to strengthen checks that core active ingredient metadata is correct
- A file for validation for NDA, ANDA – for strength and active ingredient – to make sure they are correct. Applicable to Rx and OTC products.
- Files will be posted to FDA/HHS site and be publicly available. An example file and example error message may be circulated to LT for training purposes.

Reminder to industry - Encourage companies to check that their NDA and ANDA files will validated against the Product Concept Indexing files.